PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 02-1270-A)

In application of	)	
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~~**J. Fruehauf, *et al.***~~	)	~~**Examiner: Lei Yao**~~
	)	
Serial No. 10/734,880	)	
	)	**Group Art Unit: 1642**
Filed: December 12, 2003	)	
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For: Gene Related Sensitivity and Resistance To Chemotherapeutic Drug Treatment	)	**Confirmation No.: 1031**

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-14501

RULE 132 DECLARATION OF WILLIAM RICKETTS-

APPENDIX A

William A. Ricketts, Ph.D.

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OBJECTIVE

Develop cancer diagnostics to determine the response of current drugs and companion diagnostics for new drugs that can improve the health and treatment of cancer patients.

PROFESSIONAL EXPERIENCE

Oncotech Inc – Tustin, CA

- **Vice President of Research and Chief Scientific Officer**, 2006 to present
  - Plan and manage all aspects of diagnostic development including screening, clinical validation, reimbursement, and technology review.
  - Support the sales force in selling our core clinical products to surgeons, medical oncologists, and gynecological oncologists.
  - Manage operations of our Pharmaceutical Services Division and support in sales of our services to the pharmaceutical industry.
  - Develop and maintain budgets for all four departments under my direction (Research, Clinical Research, Pharmaceutical Services, and Pharmaceutical Services Sales).
  - Represented our science, operations, and strategic advantages to the investment community.
  - Assisted in the acquisition of Oncotech by Exiqon A/S.
- **Director of Business Development**, 2005
  - Evaluated potential diagnostic tests for in-licensing to offer through our CLIA laboratory.
  - Managed operations for Pharmaceutical Services Division and support in sales of our services to the Pharmaceutical industry.
- **Pharmaceutical Services Study Director**, 2004
  - Planned and executed GLP studies in collaboration with our Pharmaceutical Services clients.
  - Wrote master service agreements, work statements, and final reports for our GLP studies.
  - Directly sold our services to the Pharmaceutical industry.

Valeant Pharmaceuticals (formerly Ribapharm) – Costa Mesa, CA

- **Project Leader**, 2000 - 2004
  - Identified new targets for anti-cancer therapies, validated their status as a target, and designed new cell based and in vitro screens.
  - Designed and validated assays for identifying protein kinase inhibitors as anti-cancer compounds.
  - Managed the anti-cancer high throughput screening effort in conjunction with Automation Biology and was responsible for the planning of all experiments to evaluate hits from HTS.

- Managed resources and integrated personnel to perform lead optimization on initial hits from primary cell based screen.
- Designed new compounds for testing in cell based and in vitro structure-activity studies.
- Managed resources and integrated personnel to perform lead optimization on initial hits from primary cell based screen.
- Completed mechanism of action studies and preliminary animal studies on an anti-cancer lead compound.
- Designed and established clinical trials protocols for an in-licensed Phase II compound.

ISIS Pharmaceuticals – Carlsbad, CA

- **Postdoctoral Fellow**, 1999 –2000
  - Identified potential new cancer drug targets by altering the expression of anti-apoptotic proteins with antisense technology to induce apoptosis in cancer cells and better understand the death signaling pathways.
  - Designed high throughput screening assays for the effects of oligonucleotides on apoptosis.

University of California San Diego – La Jolla, CA

- **Graduate Research Assistant**, Department of Endocrinology, 1994 - 1999
  - Demonstrated that the adaptor protein Shc can regulate signal transduction pathways through differential interactions with other signaling molecules.
  - Designed a series of point mutations in phosphorylation and protein-protein interaction sites to test the activity of Shc in different signaling pathways.
  - Designed, purified, and microinjected a series of recombinant proteins to ascertain the role of Shc in different signaling pathways.

University of Virginia – Charlottesville, VA

- **Laboratory Technician**, Department of Anatomy and Cell Biology, 1990 - 1994
  - Examined the role of protein phosphorylation at the chromosome kinetochore in chromosome movement and cell cycle checkpoint controls.
  - Developed several immunofluorescence labeling procedures to detect protein expression and phosphorylation on chromosomes.
  - Analyzed the potential role of gamma glutamyl transpeptidase in providing a growth advantage to cancer cells and tumors.
  - Optimized media conditions to determine if glutathione could be used by tumor cells to gain a growth advantage.

University of Virginia – Charlottesville, VA

- **Undergraduate Researcher**, Department of Microbiology, 1986-1990
  - Designed inducible mammalian expression vectors encoding mutant forms of c-src and assayed their effects on EGF signal transduction.

OTHER PROFESSIONAL EXPERIENCE

Membership in the American Association for Cancer Research

Regulatory Compliance for Biologics and Drugs Course
UCSD Extension, *University of California, San Diego*
- An introductory course to FDA regulations and compliance.

Service as a Reviewer, Journal of Biological Chemistry

EDUCATION

University of California San Diego, Department of Biomedical Sciences – La Jolla, CA
Doctorate of Philosophy, Biomedical Sciences (1999)

- Title of Dissertation: "The Roles of the Adaptor Protein Shc in Mitogenic Signaling"

University of Virginia, Department of Biology

- Bachelor of Arts, Biology (1990)

PUBLICATIONS

d'Amato, T.A., Landreneau, R.L., **Ricketts, W.A.**, et al. *Survival among patients with platinum resistant, locally advanced non-small cell cancer treated with platinum-based systemic therapy.* Journal of Thoracic and Cardiovascular Surgery. In press.

d'Amato, T.A., Landreneau, R.L., **Ricketts, W.A.**, et al. *Chemotherapy Resistance and oncogene expression in non-small cell lung cancer.* Journal of Thoracic and Cardiovascular Surgery 133:352-363.

Sharma, P.M., Son, H., **Ricketts, W.A.,** and Olefsky, J.M. *Mechanism of SHIP mediated inhibition of Insulin and PDGF-stimulated MAP Kinase activity in 3T3-L1 adipocytes.* Molecular Endocrinology 19 (2): 421-30.

Ugi, S., Sharma, P.M., **Ricketts, W.A.,** Imamura, T., and Olefsky, J.M. *Phosphatidylinositol 3-kinase is required for insulin-stimulated tyrosine phosphorylation of Shc in 3T3-L1 adipocytes.* Journal of Biological Chemistry: 277(21): 18592-18597.

Ugi, S., Imamura, T., **Ricketts, W.A.**, and Olefsky, J.M.. *Protein Phosphatase 2A forms a molecular complex with Shc and regulates Shc tyrosine phosphorylation and mitogenic signaling.* Molecular and Cellular Biology 22(7):2375-2387.

Dalle, S.F., **Ricketts, W.A.**, Vollenweider, P., Imamura, T., and Olefsky, J.M. *Insulin and IGF-I signaling differ in the involvement of G protein signaling components.* Journal of Biological Chemistry 276(19): 15688-15695.

Bannerman, D.D., Tupper, J.C., **Ricketts, W.A.**, Bennett, F.C., Winn, R.K., and Harlan, J.M. *A Constitutive cytoprotective pathway protects endothelial cells from inflammatory mediator-induced apoptosis.* Journal of Biological Chemistry 276(18): 14924-14932.

Collins, L.R., **Ricketts, W.A.**, Yeh, L., and Cheresh, D. *Bifurcation of cell migratory and proliferative signaling by the adaptor protein Shc.* Journal of Cell Biology 147(7): 1561-1568.

Ricketts, W.A., Brown, J.H., and Olefsky J.M. *Pertussis toxin sensitive and insensitive thrombin signaling to Shc and mitogenesis is mediated by different mechanisms.* Molecular Endocrinology 13(12): 1988-2001.

Ricketts, W.A., Collins, L.R., Olefsky, J.M., and Brown, J.H. *The G12 coupled thrombin receptor stimulates mitogenesis through the Shc SH2 domain.* Oncogene 15(5): 595-600.

Ricketts, W.A., Rose, D.W., Shoelson, S., and Olefsky J.M. *Functional roles of the Shc phosphotyrosine binding and Src homology 2 domains in insulin and epidermal growth factor signaling.* Journal of Biological Chemistry 271(42): 26165-26169.

Hanigan, M.H., Brown, J.E., and **Ricketts, W.A.** *Gamma-glutamyl transpeptidase, a glutathionase, is present in some cell culture grade bovine sera.* In Vitro and Cellular Developmental Biology 29A(11): 831-833.

Gorbsky, G.J. and **Ricketts, W.A.** *Differential expression of a phosphoepitope at the kinetochores of moving chromosomes.* Journal of Cell Biology 122(6): 1311-1321.

Hanigan, M.H. and **Ricketts, W.A.** *Extracellular glutathione is a source of cysteine for cells that express gamma-glutamyl transpeptidase.* Biochemistry 32(24): 6302-6.

POSTERS, PRESENTATIONS, AND INVITED TALKS

Ricketts, W.A. October 20th, 2008, San Diego, Ca. *A New Diagnostic Platform for Prediction of Drug Response Based on Tumor miRNA Profiles.* D2D IBC Meeting.

Teoh, D., Holloway, R.W., **Ricketts, W.A.**, et al. The Association of ERCC1 and Clinical Outcomes of Women with Advanced Ovarian Cancer. ASCO 2008: 5575.

Zakashanskey, K., Bradley, W.H., Rahaman, J., Dottino, P., and **Ricketts, W.A.** *Comparitive Genomic Hybridization Predicts Time to Recurrence in Primary Ovarian Cancer.* Proceedings of the Society of Gynecological Oncologists 2008.

Søkilde, R., Høiby, P.E., Smith, D.L., **Ricketts, W.A.**, Møller, S. and Litman, T.H. *A new diagnostic platform for prediction of drug response based on a tumor's miRNA profile.* AACR 48: LB-288.

Søkilde, R., Høiby, P.E., Nielsen, B.S., Møller, S., **Ricketts, W.A.**, and Litman, T.H. *Global microRNA profiling using novel miRCURY LNA™ microarrays enables identification of tumors of unknown primary origin.* Keystone Symposium: RNAi, MicroRNA, and Non-Coding RNA 2008.

Jinawath, N., **Ricketts, W.A.**, et al. *The role of NAC-1 in the development of Taxol resistant ovarian cancer.* AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics 2007.

Balasubramanian, S. **Ricketts, W.A.**, et al. *Activity of a novel HDAC inhibitor PCI-24781 in colorectal cancer: Discovery and validation of biomarkers of sensitivity and resistance.* AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics 2007.

Smith, D.L., van Waes, M., and **Ricketts, W.A.** *Correlating Signal Transduction Protein Kinase Levels, SNPs, and Drug Resistance in Human Melanoma.* AACR Proceedings 46: 925.

Covic, S., Smith, D.L., and **Ricketts, W.A.** *Detecting Altered Expression and Activation of Signaling Pathways in Cisplatin Resistant Ovarian Cancer.* AACR Proceedings 46: 1363.

Re, A. and **Ricketts, W.A.** *A 96-well Soft Agar Based Assay for Testing Cell Lines and Tumors for Drug Resistance.* AACR Proceedings 46: 1363.

Smith, D.L., Shahbahrami, B, Covic, S., and **Ricketts, W.A.** *Identification of Amplifications and Deletions in Taxol Resistant Ovarian Cancer.* Proceedings of the Society of Gynecological Oncologists. 2006.

Smith, D.L., van Waes, M, and **Ricketts, W.A.** *Optimization of protocols and screening of Topoisomerase II for SNPs that predict response to etoposide and doxorubicin.* AACR Proceedings 45: 4487.

Somberg, R., **Ricketts, W.A.**, Smith, D., and Bulliet, B. *A new universal luminescent kinase assay for HTS.* AACR Proceedings 44: 4579.

Ricketts, W.A. May 3rd, 2003, San Diego, Ca. *Developing a High Throughput Cell Based Kinase Assay.* SRI Protein Kinase Meeting.

Ricketts, W.A. Sept. 9th, 2002, Boston, Ma. *Screening a chemically diverse library with novel kinase assays.* IBC Protein Kinase Meeting.

Ricketts, W.A., Vollenweider, P., Clodi, M., Imamura, T., and Olefsky, J.M. *Insulin and IGFI signaling differ in the involvement of G protein signaling components.* Diabetes 48 (S1): 1468.

Collins, L.R., **Ricketts, W.A.**, Klemke, R., Yeh, L., and Cheresh, D. *A role for the adaptor protein Shc in cell migration on the extracellular matrix.* Molecular Biology of the Cell 9(S1): 301a.

Ricketts, W.A. and Webster, N.J. *The 66 kDa Isoform of Shc is Involved in Insulin Signaling.* Diabetes 46(S1): 279A.

Ricketts, W.A. *The role of Shc in G protein coupled receptor signaling.* University of California, San Diego, Department of Pharmacology, La Jolla, CA. (1996)

Ricketts, W.A. *Signal Transduction through the adaptor protein Shc* University of Maryland, Baltimore Co., Department of Physiology, Baltimore, MD. (1996)

Ricketts, W.A. and Olefsky, J.O. *The phosphotyrosine interaction domains of Shc interact differently in signaling by receptor tyrosine kinase and G protein coupled receptors.* Hood College Oncogene Meeting. (1996)

Morris, A.J., Haruta, T., Martin, S.S., **Ricketts, W.A.**, Gustafson. T.A., Rose, D.W., and Olefsky, J.M. *Interaction between IRS1 and the insulin receptor is required for some but not all of insulin's intracellular effects.* Diabetes 45(S1): 45A.

Ricketts, W.A., Rose, D.W., and Olefsky, J.M. *Differential Interactions of Shc phosphotyrosine binding domains in insulin and epidermal growth factor signaling.* Diabetes 45(S1): 182A.

Ricketts, W.A. and Gorbsky, G.J. *Binding of $p34^{cdc2}$ at the kinetochores of mammalian cells is cell cycle dependent and regulated by phosphorylation.* Molecular Biology of the Cell 4(S1): 118a.

Gorbsky, G.J. and **Ricketts, W.A.** *Differential phosphorylation of kinetochores in prometaphase: Possible roles in directing chromosome movement and the onset of anaphase.* Molecular Biology of the Cell 3(S1): 344a.

PATENTS

Ricketts, W.A., and Smith, D.L. *Reagents and Methods for Predicting Drug Resistance (Doxil and Gemcitabine).* US Patent Application (provisional).

Ricketts, W.A., and Smith, D.L. *Reagents and Methods for Predicting Drug Resistance (Platinums).* US Patent Application (provisional).

Kerfoot, C., **Ricketts, W.A.**, and Smith, D.L. *Reagents and Methods for Predicting Drug Resistance (Taxanes).* US Patent Application 20060160114.

Zhang, W., **Ricketts, W.A.**, An, H., and Hong, Z. *Heterocyclic compounds and uses thereof.* US Patent Application 20060205026.

Ricketts, W.A., Diaz, P. and Hong, Z. *Parallel Inducible Cell-Based Kinase Screen.* US Patent Application 20040039037.

Ackermann, E.J., Bennett, C.F., Watt, A.T., **Ricketts, W.A.**, and Dean, N.M. *Antisense modulation of c-FLIP expression.* US Patent Application 20040254137.